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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/598,468

08/31/2006

John S. Yu

67789-566

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11/05/2009

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EXAMINER

MACFARLANE, STACEY NEE

ART UNIT

PAPER NUMBER

1649

MAIL DATE

DELIVERY MODE

11/05/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/598,468	Applicant(s) YU ET AL.	
	Examiner STACEY MACFARLANE	Art Unit 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 August 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13-16, 18-32, 34-36 and 38-43 is/are pending in the application.
- 4a) Of the above claim(s) 4, 10, 11, 13-16, 18-32, 41 and 42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-9, 34-36, 38-40 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Claims 11, 13, 18, 34, 35 and 39 have been amended, claims 40-43 are newly added, as requested in the amendment filed on August 12, 2009. Following the amendment, claims 1-11, 13-16, 18-32, 34-36 and 38-43 are pending in the instant application.

Claims 4, 10, 11, 13-16, 18-32 and 41-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed on March 27, 2009.

Claims 1-3, 5-9, 34-36, 38-40 and 43, in so far as they read upon the elected species of A2B5 as the astrocytic marker, IL-12 as the heterologous gene and GBM and the disease/condition, are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on August 12, 2009 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112 (Withdrawn)

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 2 and 5-8 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn. Applicant has persuasively argued that the terms "markers characteristic of a precursor for astrocytic" differentiation and "heterologous gene", while both broad, were known in the art at the time of filing.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. As currently amended, Claims 1-3, 5, 6, 34-36, 38-40 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by the Lapidot et al. patent (2000) cited in the previous Office action, as evidenced by Ratajczak et al., Leukemia, 18:29-40, published October 2003.

On pages 9-10 of Remarks filed August 12, 2009, Applicant traverses the rejection of the claims as being anticipated by Lapidot et al. on the grounds that "Lapidot et al. focuses squarely on isolation of CXCR4+ hematopoietic stem cells" (page 9) but "the allegation that neural stem cell subtypes are inherent features of stem cells" is insufficient. While this has been considered in full, it is not found persuasive for the following reasons.

Claims 1-3, 5, 6, 34-36, 38-40 and 43 are drawn to product-by-process, namely, an isolated neural stem cell. The cells are further characterized by their properties:

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either exhibiting a CXCR4 receptor or demonstrating an affinity for the chemokine SDF-1, or both (it should be noted that SDF-1 is the ligand for the CXCR4 receptor); exhibiting markers characteristic of a precursor for astrocytic differentiated stem cells; exhibiting the glycoprotein A2B5; and not expressing EAAT1/EAAT2.

The rejection over Lapidot et al. is based upon the express, implicit, and inherent disclosures of the prior art reference. As stated in the previous Office action, where Applicant has claimed a composition of matter in terms of a property or characteristic and the composition of the prior art is identical or substantially identical in structure or composition but the characteristic is not explicitly disclosed by the reference, a *prima facie* case of either anticipation or obviousness has been established and the burden of proof rests upon the Applicant to demonstrate that the prior art does not necessarily or inherently possess the characteristics of Applicant's claimed product.

The Lapidot et al. prior art Patent teaches cell compositions consisting of hematopoietic CXCR4-positive progenitor and stem cells that are responsive to SDF-1. The Lapidot et al. Patent also explicitly teaches these cells wherein they further comprise a heterologous gene useful for the treatment of disease, including malignant forms of cancer.

The Ratajczak reference is relied upon as evidence that hematopoietic stem cells inherently express early neural stem cell markers and specific markers characteristic of astrocytic differentiation, such as GFAP and nestin (Figures 2 and 3). The reference further illustrates that the capability of differentiation into neural cell fates is an inherent feature of CXCR4+ hematopoietic stem cells (Figures 4 and 7) and that SDF-1 plays a

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key role in the differentiation of CXCR4+ stem cells for tissue/organ repair throughout the body (Figure 9).

Thus, the evidence demonstrates that the isolated neural stem cell product of the instant claims fails to distinguish over those described by the Lapidot et al. prior art. While the Lapidot reference does not specifically characterize the cells as exhibiting the A2B5 marker or specifically not expressing EAAT1/EAAT2, as claimed, the cells of the invention and those of the art are substantially identical, therefore, the properties or characteristics they exhibit (A2B5) or do not exhibit (EAAT1/EAAT2) are merely inherent features.

Where the claimed and prior art products are identical or substantially identical in structure or composition the burden of proof rests upon the Applicant to demonstrate that the prior art does not necessarily or inherently possess the characteristics of Applicant's claimed product. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the claims 1-3, 5, 6, 34-36, 38-40 and 43 are rejected.

7. As currently amended, Claims 1-3, 34, 39, 40 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Lazarini et al., *Europ J of Neurosci*, 12:117-125, 2000.

Claims 1-3, 34, 39, 40 and 43 are drawn to product-by-process: An isolated neural stem cell isolated by a method comprising selecting said cell based on exhibiting a CXCR4 receptor or demonstrating an affinity for the chemokine SDF-1, or both (it should be noted that SDF-1 is the ligand for the CXCR4 receptor); exhibiting markers characteristic of a precursor for astrocytic differentiated stem cells; exhibiting an A2B5 marker; and not expressing EAAT1/EAAT2.

Lazarini et al. teach neural progenitor cells that are CXCR4+ (Figure 2), responsive to SDF-1 (Figures 4 and 6), and exhibit markers that are characteristic of astrocytic differentiation, such as GFAP and nestin (Figure 1). While the Lazarini reference does not specifically characterize the cells as exhibiting the A2B5 marker nor as specifically not expressing EAAT1/EAAT2, as claimed, the cells of the invention and those of the art are substantially identical, therefore, the properties or characteristics they exhibit (A2B5) or do not exhibit (EAAT1/EAAT2) are merely inherent features.

Where the claimed and prior art products are identical or substantially identical in structure or composition the burden of proof rests upon the Applicant to demonstrate that the prior art does not necessarily or inherently possess the characteristics of Applicant's claimed product. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the claims 1-3, 34, 39, 40 and 43 are rejected.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. As currently amended, Claim 9 stands as rejected under 35 U.S.C. 103(a) as being unpatentable over Lapidot et al., as applied to claims 1-3, 5, 6, 34-36, 38-40 and 43 above, and further in view of Tahara et al., (1994).

Claim 9 is drawn to an isolated stem cell selected for exhibiting CXCR4 and/or SDF-1 affinity and further comprising a heterologous gene encoding a polypeptide for the treatment of a disease condition involved in immune response, wherein said polypeptide is IL-12.

On page 13 of Remarks (*Id*), Applicant traverses the rejection on the grounds that "Neither Tahara et al. nor Lapidot et al. provides sufficient detail to achieve the

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present invention of CXCR4+ Neural stem cells heterologously expressing IL-12." This has been carefully considered but is not found persuasive for the following reasons.

As stated above, the product of the claims is identical or substantially identical in structure or composition to that disclosed by Lapidot et al. The Lapidot reference further explicitly teaches methods for the expression of heterologous genes useful in the treatment of disease, including malignancies.

The Lapidot et al. art is only silent with respect to heterologous expression of IL-12, however, the Tahara et al. prior art teaches that it was well-known in the art prior to the time of the instant invention that cells genetically engineered to secrete IL-12 can suppress tumor growth in vivo. Therefore, Examiner maintains for reasons of record, that the invention as a whole is *prima facie obvious*, if not actually anticipated by the reference.

Conclusion

11. No claim is allowed.

12. This application contains claims drawn to an invention nonelected with traverse in Paper filed on 3/27/2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-W and F 5:30 to 2, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/John D. Ulm/
Primary Examiner, Art Unit 1649